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Evaluation of medication-assisted treatment of opioid dependence : the physicians' perspective

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Abstract: **BACKGROUND:** There is controversy about which outcome parameters should be employed to assess substance use treatment. Subjective measures of medication-assisted treatment (MAT) of opioid dependence are increasingly important. However, while patients' perspectives have been examined, the caregivers' views remain largely unknown. Here, we explore how physicians evaluate MAT, and which predictors are most relevant. **METHODS:** We conducted a retrospective cohort study of all MAT episodes with oral opioid agonists in the canton of Zurich between 1998 and 2013 using a case register. Termination forms of the register include a physician-completed assessment on the course of the treatment episode. Mixed model analysis was applied to determine relevant predictors. **RESULTS:** The analysis was based on 17,234 episodes from 7432 patients. Mean global assessment of the course of MAT was 'moderate'. The most important predictors for treatment evaluation by physicians were treatment break off as reason for termination ($p < 0.0001$), psychological improvement throughout treatment ($p < 0.0001$), wish for abstinence from the substitute ($p < 0.0001$), social integration index at termination ($p < 0.0001$), and social ($p < 0.0001$) as well as medical ($p < 0.0001$) improvement. The negative association of treatment break off with MAT assessment was more pronounced in semi-rural than urban areas ($p < 0.0001$). **CONCLUSION:** Predictors relating to the well-being and functioning of the patient as well as the reasons underlying treatment termination appear to be more important for the treating physician's evaluation of medication-assisted treatment episodes than on-going substance use. Coming off the opioid medication plays a central role, independent of ongoing illicit substance use.

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Evaluation of medication-assisted treatment of opioid dependence – the physicians’ perspective*

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ABSTRACT

Background: There is controversy about which outcome parameters should be employed to assess substance use treatment. Subjective measures of medication-assisted treatment (MAT) of opioid dependence are increasingly important. However, while patients' perspectives have been examined, the caregivers' views remain largely unknown. Here, we explore how physicians evaluate MAT, and which predictors are most relevant. **Methods:** We conducted a retrospective cohort study of all MAT episodes with oral opioid agonists in the canton of Zurich between 1998 and 2013 using a case register. Termination forms of the register include a physician-completed assessment on the course of the treatment episode. Mixed model analysis was applied to determine relevant predictors. **Results:** The analysis was based on 17,234 episodes from 7,432 patients. Mean global assessment of the course of MAT was 'moderate'. The most important predictors for treatment evaluation by physicians were treatment break off as reason for termination ($p < 0.0001$), psychological improvement throughout treatment ($p < 0.0001$), wish for abstinence from the substitute ($p < 0.0001$), social integration index at termination ($p < 0.0001$), and social ($p < 0.0001$) as well as medical ($p < 0.0001$) improvement. The negative association of treatment break off with MAT assessment was more pronounced in semi-rural than urban areas ($p < 0.0001$). **Conclusion:** Predictors relating to the well-being and functioning of the patient as well as the reasons underlying treatment termination appear to be more important for the treating physician's evaluation of medication-assisted treatment episodes than on-going substance use. Coming off the opioid medication plays a central role, independent of ongoing illicit substance use.

KEYWORDS: Maintenance therapy; replacement therapy; subjective; heroin; opiate; provider; predictor

1. INTRODUCTION

Opioid dependence is a chronic disorder characterized by relapse and rare long-term cessation (Genberg et al., 2011; Termorshuizen, 2005). It often entails negative sequelae for the affected individuals and their families, and substantial public health consequences for society as a whole (Whiteford et al., 2013). In 2014, the prevalence of opioid dependence was estimated at 0.4% for the European Union (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2014). Medication-assisted treatment (MAT) with methadone, l-polamidone, buprenorphine or slow-release oral morphine sulphate is considered to be the treatment of first choice (Dole and Nyswander, 1965; Mattick et al., 2014, 2009; Ward et al., 1999; WHO, 2009). Due to the chronicity of opioid dependence, current treatment guidelines favor the open-end nature of MAT, sometimes required to continue lifelong (APA, 2006; Swiss Society of Addiction Medicine (SSAM), 2013). In some countries, legal regulations still call for complete abstinence (including opioid substitutes) as mandatory treatment goal, but abstinence-oriented therapy is often unsuccessful due to high relapse rates with the risk of deteriorating psychosocial conditions or even death due to overdose after lost tolerance to opioids (Caplehorn et al., 1994; Merrall et al., 2010; Strang, 2003). The rate of spontaneous or professionally assisted remission remains controversial. A recent review found a rate of 9% annually (Calabria et al., 2010). Typically, however, when access to MAT is low-threshold, many opioid-dependent patients enter and leave treatment repeatedly in the course of their disorder (Bell et al., 2006), which, among other reasons (such as changing the responsible physician), may reflect patients' desire for more independence and 'getting clean', i.e., complete abstinence including the substitute (Gutwinski et al., 2014; Winstock et al., 2011). There has been intensive debate on suitable outcome parameters in the evaluation of substance use treatment in general, and MAT in particular (Bühringer, 2012; Donovan et al., 2012; Tiffany et al., 2012; Uchtenhagen, 2012). MAT is associated with a reduction in substance use, mortality, treatment dropouts, HIV infections, psychosocial symptom load and

delinquency, and an overall increase in quality of life (Brugal et al., 2005; Cacciola, 2001; Deck et al., 2009; Feelemyer et al., 2014; MacArthur et al., 2012; Mattick et al., 2009). Most treatment studies focused on putative objective parameters, while the subjective outcomes of MAT have received less attention. However, there is an increasing recognition that these constitute essential measures of MAT quality (Tiffany et al., 2012; Trujols et al., 2011; Uchtenhagen, 2015). Few studies have investigated subjective views of MAT episodes (Montagne, 2002; Stancliff, 2002), and, if so, mostly addressed patient satisfaction (Kelly et al., 2010; Marchand et al., 2011; Trujols et al., 2012). Fewer studies still have investigated the views of treatment providers (Becker and Fiellin, 2006). These mostly concentrated on meta-aspects, such as the provision of MAT and harm reduction (Deren et al., 2011; Forman et al., 2001; Notley et al., 2014), barriers to care (Schulte et al., 2013), the diversion and misuse of the substitute (Larance et al., 2011), reasons for dropout and treatment retention (Gutwinski et al., 2014) or combinations of the above (Besson et al., 2014). To our knowledge, Trujols et al. (2011) conducted the only study investigating both provider and patient views of single MAT episodes (Trujols et al., 2011). Using patient and clinician versions of the Global Impression of Improvement Scale in a sample of 110 MAT patients, they demonstrated that patients and providers often have discordant perceptions of improvement in treatment (Trujols et al., 2011). It remains unclear, however, which predictors determine physicians' assessments of MAT course and whether these are similar to the outcomes used in MAT evaluation. They reflect on providers' implicit treatment goals and conceptualisation of MAT, which may differ from those of patients, public health policy makers or researchers investigating MAT. Relevant predictors may be based on personal biases as well as scientific evidence and legal regulations. They may influence attitude towards the patient, and physician as well as patient behavior, such as the decision to enter, stay in or leave treatment, or shared-decision making during treatment.

The aim of this study was to determine the predictors of physicians' assessment of MAT using data from Zurich, Switzerland.

2. METHODS

Zurich is both the most populous Swiss canton and the largest Swiss city. Following the development of open drug scenes, harm reduction measures were scaled up massively in the 1990s. MAT has since been offered on a low-threshold basis with opioid dependence as single entry criterion and wide accessibility. It is reimbursed by mandatory health insurance, and patients can freely choose their provider. Since 1991, the canton monitors MAT with methadone, buprenorphine, and recently slow-release oral morphine sulphate, with an anonymized treatment case register (Nordt and Stohler, 2006). Heroin-assisted treatment is excluded and evaluated separately. Physicians are required to complete a questionnaire at initiation and termination of treatment, as well as twice yearly or when changing the substitute. Collection and evaluation of data are in accordance with the data protection law of the canton of Zürich and the local ethics committee approved the analysis.

For analysis of clinicians' evaluation of treatment episodes, we used the question on "global assessment of treatment course", which physicians answered on a five-point Likert scale (1 "very unfavorable", 2 "rather unfavorable", 3 "moderate", 4 "rather favorable", 5 "very favorable") at termination of treatment.

The question on reasons for treatment termination in the evaluation questionnaire could originally be answered in seven ways: 1 "regular, abstinent (from substitute)", 2 "regular, in mutual consent", 3 "formal break off by patient", 4 "formal break off by physician", 5 "loss of contact", 6 "patient deceased" and 7 "other (to be specified)". For the multivariate analysis, we grouped those answers as follows: abstinent (option 1), regular (including option 2, 6 and 7), and treatment break off (option 3, 4 and 5). Physicians were also asked to report *changes* in psychological, medical and social conditions of the patient throughout treatment and could answer on a three-point scale 1 "worsened", 2 "unaltered", 3

“improved”. Moreover, we used data from the entry questionnaire on these conditions, coded 1 “(rather) bad”, 2 “moderate”, 3 “(rather) good”. Using the mean of at least four of six items (having a full or part time job, earning one’s living; living in a flat; having a partnership; good family relations; having friends outside the drug scene) we calculated a social integration index, ranging between 0 and 1 (Cronbach’s Alpha = 0.58).

Furthermore, the questionnaire comprised items on the use of heroin, cocaine, illicit benzodiazepines and alcohol in the past 30 days before treatment termination, each answered on a four-point scale coded 1 “none”, 2 “occasionally”, 3 “(almost) daily”, 4 “several times a day”. We also used data on age of onset of heroin use (dichotomized as 18 years or earlier versus 19 years or later), duration of opioid use (in decades) and lifetime intravenous use. Moreover, we included age (in decades and centered at 30 years), number of MAT episodes and duration of current episode (in months, logarithmized) as predictors. Finally, treatment providers were characterized by type (private practice versus specialized institution) and by area. The latter was operationalized as “urban”, corresponding to the city of Zurich, or “semi-rural”, corresponding to the surrounding canton.

Between 1991 and the end of October, 2014, 34,082 treatment episodes of 11,749 patients were collected. A careful check for overlapping treatment episodes led to the exclusion of 201 episodes. Although we used information of all entry forms for each patient, gender (6%), ever injecting status (8%), and nationality (13%) remained unknown for some patients. For about 28% of patients we could not obtain a plausible year of first regular heroin use (not before their 12th year of age, not after their first MAT according to our case register, difference in cases of multiple entry forms three years or less; Nordt and Stohler, 2006). As there were also missing data in time-dependent predictors that are most likely correlated within individuals (e.g., frequency of drug use, social integration), we applied the multiple imputation procedure of SPSS 22 in addition to a complete case analysis that could only use

about 26% of the available data. We did not impute reasons of cessation, as some may occur repeatedly in a patient except in the case of death.

As our case register is far from being a balanced repeated-measure dataset – where all patients provide the same number of follow-up datasets within the similar time period – we applied a two-stage approach. The first stage included invariant personal characteristics where we used the mean value of all predictors of our model of interest (MOI), with fully conditional specification including one-way interactions for nominal predictors (i.e., gender, nationality, and injecting status). The number of imputed datasets was set to ten. The third predictor requiring imputation on the first stage was year of first regular heroin use which was also checked for plausibility as described above, and in order to keep consistency, we made small correction where appropriate (< 2% of all imputed values). The second-stage imputation used for all time-dependent MOI variables additional ‘difference variables’ (indicating the difference of an observed value to the person’s specific mean value of the first stages) for each first-stage imputed dataset separately. Finally, the imputed values of treatment evaluation, change in psychological, medical and social condition, of frequency of drug use, social integration, initial psychological, medical and social condition were calculated by the imputed mean and difference value that was converted into outcome categories. Similarly, if the imputed values of the social integration index were outside the range of 0-1, they were set to the respective limit value.

We used mixed models analysis in SAS 9.4 for the MOI of treatment evaluation with patient ID as repeated subject identification. The analysis was only applied on treatment episodes that ended between January 1st, 1998 and December 31st, 2013, as frequency of drug use was not part of cessation forms before 1998. The selection criteria described above resulted in a total of 20,146 datasets from 8,002 patients. A valid value of treatment evaluation was present in 14,574 episodes, but a reason given for treatment cessation was obtained from 17,247 episodes. We report the mixed model analysis results for the imputed

dataset but also provide the results of the complete dataset (see supplementary table¹) as multiple imputation has both potential and pitfalls (Sterne et al., 2009). Interactions were tested with reasons of MAT termination, and provider location and type, but only significant results are reported.

3. RESULTS

Unless otherwise indicated, all results reported refer to the imputed dataset. The annual number of discontinued MAT episodes declined rather linearly from 1,773 in 1998 to 847 in 2013, with slight transient increases in 2003, 2004 and 2008 (Figure 1). Seventy-one per cent of patients in our dataset were male. Patient nationality was Swiss in 79%, a number comparable to other Swiss studies (Baumeister et al., 2014). While data on ethnicity is not collected in the register, most non-Swiss patients are from European countries and therefore also of Caucasian ethnicity. Mean age at termination was 32 years. The median duration of treatment episodes was 199 days. The duration was longest for the fourth episode with 249 days and slightly decreased for further episodes. The mean number of episodes per patient was 2.3, with a maximum of 26 episodes. The majority of episodes were conducted in Zurich-city (60%) as opposed to semi-rural areas of the canton (40%). Physicians in private practice were involved in fifty-four per cent of the MAT episodes, whereas 46% worked in institutions. There were 4434 and 4840 treatment episodes from 187 and 327 different private practices in urban versus semi-rural areas, respectively. Concerning institutions, we registered 7656 and 3216 treatment episodes from 16 and 15 institutions in urban and semi-rural areas, respectively.

Figure 2 depicts the mean scores of MAT physicians' global assessment of treatment course by year. It can be seen that they remain very stable over the years, ranging between 2.92 (2002) and 3.15 (2013), corresponding to a “moderate” value overall.

¹ Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:...

Physician-reported reasons for treatment termination over time are depicted in figure 3. Most prevalent for the whole study period was the reason “regular, in mutual consent” (40.5%). Its frequency was highest at 47% in 2005 and declined somewhat afterwards with a slight increase in years 2008, 2010 and 2013. The second most prevalent reason was “loss of contact” (24.9%), peaking at 33% in 2000 and declining to 18% in 2013. It is followed by “abstinence” (12.6%), which was most common in 1999 with 18%, declining to 10% in 2007 and again increasing to 15% in 2013. Less common reasons were “formal break off by patient” (10.1%), and “formal break off by physician” (5.9%). The proportion of death as reason for termination (4.3%) has been increasing steadily since 1998. This finding is mostly connected to the decreasing annual number of overall treatment cessations during the study period (Figure 1). Actually, the number of deaths per person years in treatment remained rather constant throughout the study period between 1998 and 2013. “Other” reasons were rare (1.6%).

The mixed-model analysis overall included 17,234 episodes of 7,432 patients. Due to the size of the dataset most p-values are small. Model 1 shows that the physician assessment of treatment course was almost 1 point elevated if the reason for MAT termination was “abstinent”, irrespective of whether the physician worked in a semi-rural or an urban area. In cases with a break off as reason for MAT termination, this lead to a poorer assessment score (-0.68) for physicians in semi-rural than for those in urban areas (-0.68+0.25=-0.43). Physician assessment of treatment course showed no difference between both areas in cases with regular termination. In contrast to area, the type of the institution (private practice versus specialized institution) did not interact with reason for MAT termination. Besides the two physician variables, model 2 included a broad variety of patient characteristics that showed similar estimates as in model 3, in which predictors of model 1 were added. In contrast, the estimate for ‘abstinent’ in model 3 is substantially lower with 0.38 than in model 1 with 0.95. The strongest association in model 3 was observed for treatment break off as reason for MAT

termination (negative), followed by change in psychological condition throughout the MAT episode, abstinence as termination reason, the social index score at termination, and change in social and, albeit smaller, medical condition (all positive). In model 3, there was still a relevant interaction between area and treatment break off, with a less negative effect of treatment break off on MAT evaluation in urban compared to semi-rural areas. The detailed results of the analysis are displayed in Table 1.

4. DISCUSSION

To our knowledge, this is the first study providing insights into how physicians judge the success of MAT episodes in clinical practice. The overall “moderate” evaluation across the whole sample calls into mind the chronicity and complexity of the treatment of opioid dependence (McLellan et al., 2000). Our findings are of particular interest in light of the debate about which outcome parameters to apply in the assessment of substance use treatment (Bühringer, 2012; Donovan et al., 2012; Miller and Miller, 2009; Tiffany et al., 2012; Uchtenhagen, 2015). Some researchers have argued that substance use is the most suitable parameter for treatment success and should thus be the primary outcome of treatment evaluation (Donovan et al., 2012). However, in our study the concomitant use of substances only had a small effect. The most important predictors that we identified relate to psychological and medical patient health, social integration and the circumstances of treatment termination. MAT providers seem to apply broad criteria, targeting various facets of patients’ well-being, and prescription and dispensing of the substitute are ideally accompanied by psychosocial and medical interventions. While the concentration on substance use as primary outcome parameter may have its merits in the comparative evaluation of different maintenance agonists, it may be insufficient when evaluating MAT as a whole in clinical practice, and is not reflected in the predictors influencing clinicians’ evaluation which we identified.

The physician's perception of improvement of the patients' psychological condition throughout MAT was of great importance for the evaluation of the MAT course, as were, albeit to a lesser extent, social and medical improvement. The relevance of psychological improvement as a treatment goal of providers in general addiction treatment has been described in a recent study by Joosten et al. (2011). These perceptions likely reflect an improvement in health as well as in social reintegration. Furthermore, given the high proportion of opioid dependent patients with comorbid psychiatric disorders, the reduction of psychopathological symptoms is a legitimate and important goal of treatment. It is increasingly recognized that outcomes reflecting these changes, such as psychosocial symptom burden or quality of life measures, should be included in studies on the effectiveness of substance use treatment (Nosyk et al., 2011). Our findings underline the importance of these parameters in clinical practice.

We used the information on social integration to calculate an index score from several separate predictors. This composite score includes details on work, living conditions and social relations at the time of MAT termination. It shows a strong positive relationship with treatment evaluation, emphasizing the significance of social reintegration in the evaluation of MAT. Social functioning has also been associated with patients' satisfaction with MAT (Trujols et al., 2012), and may therefore constitute an important common outcome parameter for patients as well as providers. Of course, as we collected no data on this, we cannot rule out that socially well-integrated patients are less likely to suffer from psychiatric comorbidities. Such comorbidities may negatively affect treatment course as well as interaction with treatment providers. Physicians may also be more likely to judge these patients as 'difficult' or hard-to-treat, and MAT itself as less successful.

In our study, circumstances underlying MAT termination were grouped as "abstinent" (i.e., coming off the substitute), "regular" (including mutual consent and patient death) and "break off" (premature termination due to patient or provider initiative or loss of contact). The

strongest predictor in our final multivariate model was treatment break off, which had a negative effect compared to regular termination of MAT. Break off may occur for various reasons on the patients' as well as the physicians' side. For instance, it may occur due to the desire for more independence, of medication or the sometimes rigid MAT setting. For some severely disintegrated comorbid patients, the requirements of regular, daily to weekly appointments to collect the substitute may be too demanding. Break off may also result from difficulties in the therapist-patient relationship, repeated breaking of rules or even violent threats or behaviors. Most likely, premature termination of MAT will occur in a situation where not all treatment goals (whatever these are) have been reached, which could further explain the negative association.

This association was stronger for semi-rural than urban areas. Treatment in semi-rural areas may be less anonymous, and long-term personal knowledge between provider and patient may be more common in these closer-knit settings, possibly leading to a more severe judgment of irregular treatment cessation and more associated concerns. Because there are fewer providers in semi-rural areas, the possibilities for a patient to reinitiate MAT with a different provider may be limited as compared to urban areas, making treatment break off more significant as patients may end up with insufficient care. There are also reports about stronger stigmatization of substance users by the general population as well as mental health professionals in more rural settings (Oser et al., 2013; Yannessa et al., 2008), which may lead to more negative assessments.

Generally, the relevance of this predictor is consistent with the use of treatment dropout as outcome parameter in trials investigating the effectiveness of MAT. While MAT is very effective in retaining patients in treatment, abrupt termination for a variety of reasons remains problematic from the providers' view. These findings may reflect the medical conceptualization of MAT as an often open-end long-term treatment of a chronic disorder.

Abstinence (i.e., stopping or tapering the substitute opioid, ‘getting clean’) as reason for termination of MAT equally showed a strong association (even the strongest in bivariate analysis): When patients were coming off the substitute, providers were likely to rate the treatment course more positive than with other regular circumstances of treatment cessation.

In the past three decades, the view on abstinence has changed from the ultimate goal of treatment to one possible option among others in maintaining well-being of the patient (Uchtenhagen, 2013). This is also reflected in the current MAT recommendations of the Swiss Society for Addiction Medicine, which endorse a long-term, open-ended approach and recommend exploring with the patient the advantages and disadvantages of abstinence from the substitute (Swiss Society of Addiction Medicine (SSAM), 2013). While we did not find evidence for a change of the effect of abstinence on treatment evaluation with time since 1998, our findings illustrate that it remains an important option in the treatment of opioid dependence. One may argue that the positive association does not reflect the value of abstinence per se, but rather other factors, such as the mutual consent about treatment goals or the stable situation of a patient deciding to come off the substitute in agreement with the responsible physician. However, these factors were also applicable for those MAT episodes with other regular reasons for termination in mutual agreement. The effect remained significant when controlling for substance use in the last 30 days of the MAT episode. Thus, even if patients were still using illicit drugs, physicians rated the treatment course more favorable when patients opted for tapering of the opioid substitute. Moreover, we statistically controlled for a wide variety of other predictors such as duration of treatment and, most importantly, improvement of social, medical and psychological conditions as perceived by the physician. Future research could investigate the role abstinence plays for MAT-providing physicians in more detail with qualitative methods.

There has been increasing advocacy for a patient-centered approach in MAT taking into account the preferences and resources of the patient during treatment, and subjective

well-being and quality of life for outcome research (Miller and Miller, 2009; Uchtenhagen, 2015). The strong association of physician-perceived course of treatment with abstinence as reason for MAT termination may be the very expression of such a patient-centered approach, since clinical experience as well as studies show that the desire to come off MAT is still very widespread among patients (Gutwinski et al., 2014; Winstock et al., 2011). It may reflect the wish to be independent and less restricted by the necessity for regular medication use or the occasionally rigid treatment settings. Furthermore, unlike some other health systems, it is unproblematic to re-enter treatment in Switzerland when abstinence from the substitute fails, lowering the threshold to explore other, drug-free, treatment options in accordance with the patient and his individual situation.

4.1 Strength and limitations

Our study has certain limitations. It is based on routine data with missing values and we cannot completely rule out that there is a systematic pattern related to treatment evaluation. Furthermore, we did not have information on the providing physicians' specialty (psychiatry vs. GP). Due to the nature of our treatment register, all data were provided by the respective physicians responsible for MAT. As such, predictors and assessment may be influenced by personal biases. Although we are explicitly investigating subjective measurements rather than objective outcomes, having some putative objective parameters collected by independent third parties would be a valuable supplement for the future. Finally, as this study is based on questionnaires completed at termination of MAT, it does not include currently on-going MAT episodes. Among these, there may be some with highest continuity i.e., running for a long time with the same physician and the same opioid substitute. These subjects with high adherence may be rated more favorable.

Among the strengths of this study is the incorporation of data from a large number of MAT episodes and patients over a long period of time across different providers (institution-based and private practice; urban and semi-rural). Furthermore, we statistically controlled for

a multitude of predictors by using mixed model analysis. Finally, our study considers the evaluation of whole MAT episodes, as opposed to outcomes at certain time points after initiation, which may be less adequate for chronic disorders.

4.2 Conclusion

Our results provide novel insights into the way treating physicians evaluate the course of MAT in their patients. The mean assessment values at the end of treatment episodes were moderate. We identified several important predictors, which shed some light on the parameters MAT providing physicians apply when judging the success or failure of their treatment. Among them are psychological, social and/or medical improvements, social integration, and the reasons underlying treatment termination, namely treatment break off or coming off the substitute. Some, but not all, of these predictors are in agreement with the commonly used outcome parameters of MAT evaluation studies, such as treatment retention, substance use or psychosocial well-being.

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FIGURE LEGENDS

Figure 1 Number of terminated medication-assisted treatment episodes by year.

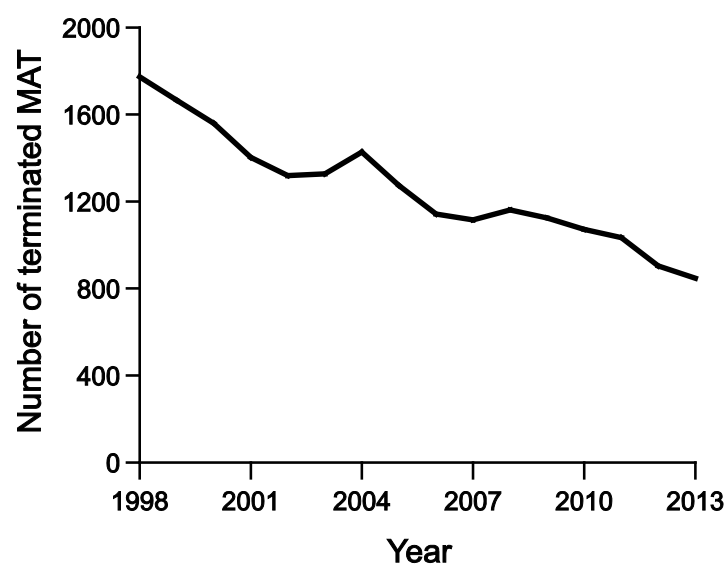


Figure 2 Treatment evaluation at termination of medication-assisted treatment, 1998-2013 (1 “very unfavorable”, 2 “rather unfavorable”, 3 “moderate”, 4 “rather favorable”, 5 “very favorable”).

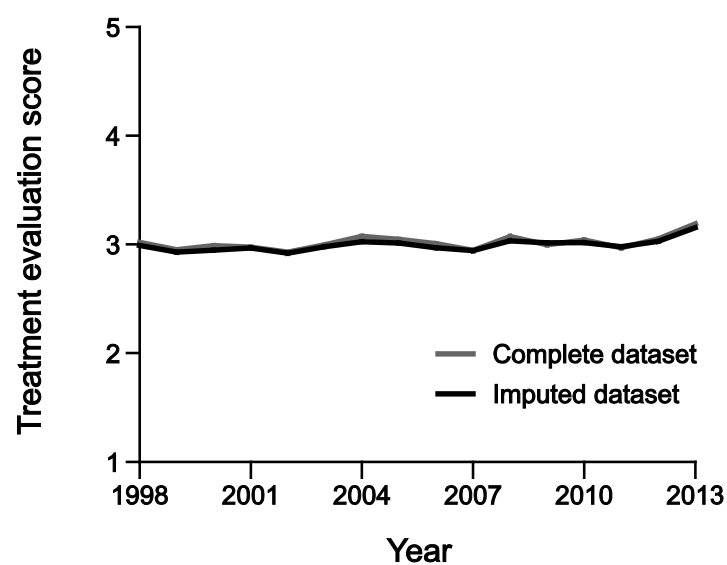


Figure 3 Physician-reported reasons for termination of medication-assisted treatment episode from 1998 until 2013.

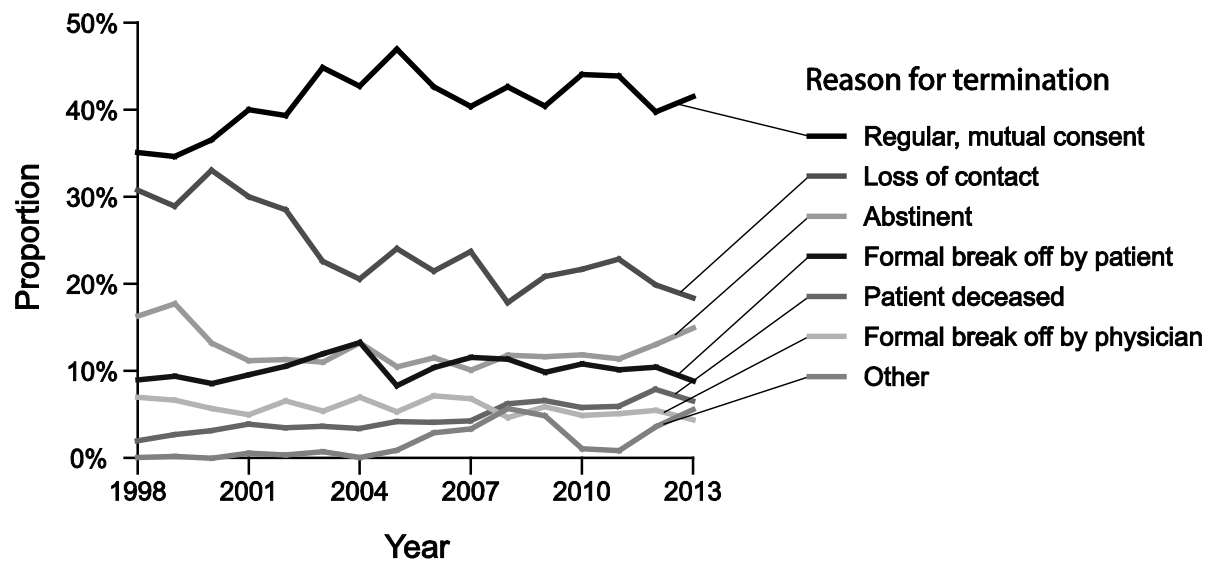


Table 1 Mixed model analysis for physicians' assessment of treatment course (imputed dataset).

	Model 1			Model 2			Model 3		
	Imputed dataset			Imputed dataset			Imputed dataset		
Reason for MAT ¹ termination	Estimate	SE	P	Estimate	SE	P	Estimate	SE	P
intercept	3.13	0.02	<.0001	0.64	0.06	<.0001	1.01	0.06	<.0001
abstinent	0.95	0.03	<.0001				0.38	0.03	<.0001
break off	-0.68	0.03	<.0001				-0.47	0.02	<.0001
Urban ³ *abstinent	-0.08	0.04	0.0701				-0.06	0.04	0.0951
urban ³ *break off	0.25	0.03	<.0001 (City)	0.04	0.02	0.0054	0.20	0.02	<.0001
urban ³ *regular	0.04	0.02	0.0887				0.01	0.02	0.6631
Institution versus private practice				0.08	0.02	<.0001	0.07	0.02	<.0001
Change in psychological condition				0.52	0.01	<.0001	0.44	0.01	<.0001
Change in medical condition				0.17	0.02	<.0001	0.16	0.02	<.0001
Change in social condition				0.29	0.02	<.0001	0.26	0.02	<.0001
Social Index Score at termination				0.39	0.03	<.0001	0.35	0.03	<.0001
Treatment duration (ln of months)				0.04	0.00	<.0001	0.04	0.00	<.0001
Use of heroin ⁴				-0.11	0.01	<.0001	-0.07	0.01	<.0001
Use of cocaine ⁴				-0.05	0.01	0.0002	-0.04	0.01	0.0025
Use of benzodiazepines ⁴				-0.05	0.01	<.0001	-0.05	0.01	<.0001
Use of alcohol ⁴				-0.03	0.01	0.0082	-0.03	0.01	0.0061
Psychological condition at treatment entry				0.06	0.01	<.0001	0.06	0.01	<.0001
Medical condition at treatment entry				0.05	0.01	<.0001	0.05	0.01	<.0001
Social condition at treatment entry				0.09	0.01	<.0001	0.08	0.01	<.0001
Number of MAT ¹ episodes				-0.01	0.00	<.0001	-0.01	0.00	<.0001
Age (in decades, rescaled 30 years)				0.05	0.02	0.0298	0.04	0.02	0.0895
Onset with 18 years or younger				0.02	0.03	0.5203	0.01	0.03	0.6572
Duration of opioid use				0.00	0.03	0.8959	0.00	0.02	0.9919
Lifetime history of injection use				0.02	0.02	0.3836	0.00	0.02	0.9986
N episodes	17234			17234			17234		
N patients	7432			7432			7432		
Max episodes of patient	26			26			26		

-2 Log-Likelihood	46940.1	(SD=54.0)	42370.2	(SD=70.1)	41163.4	(SD=89.5)
BIC	46958.0	(SD=54.1)	42388.0	(SD=70.1)	41181.3	(SD=89.5)
Covariances						
Patient	0.27	(SD=0.00)	0.16	(SD=0.00)	0.14	(SD=0.00)
Residual	0.69	(SD=0.00)	0.56	(SD=0.00)	0.52	(SD=0.00)

¹MAT = medication-assisted treatment; ²with “regular, in mutual consent” as reference category; ³urban versus semi-rural; ⁴during 30 days before discontinuation of medication-assisted treatment episode